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Cancer of Lung.—Twenty-five cases of primary carcinoma of the lung demonstrated by complete autopsy showed 13 cases of squamous epithelioma, 6 of small-cell carcinoma, 4 of adenocarcinoma, and 2 of carcinoma simplex. The age-incidence lay between 38 and 76; that of the small-cell cancer group between 40 and 72. Of the latter 4 were in males and 2 in females. The duration of the disease in the whole group was from ten days to twenty-eight months. The outstanding symptoms were moderate anaemia, leucocytosis, fever, cough, weakness, anorexia, dyspnoea, haemoptysis, and pain in the chest. The symptoms were essentially the same in the general group and the small-cell carcinoma group. The correct clinical diagnosis was made in 10 of the 25 cases. One of the small-cell carcinomata was discovered only on microscopic examination. Of the other 5, two showed multiple small nodules throughout the lung, while the other 3 were masses 6 to 12 cm. in diameter near the hilum. The tumors were of grayish color, clearly invasive, firm, cut with resistance and showed a firm, pale or yellowish gray, moist cut surface. In the small-cell series extrathoracic metastasis was more frequent than in the other types. Only 4 of the other 19 cases involved the mediastinum, while 3 of the 6 small-cell cases showed marked involvement of that region. The situation was in the upper posterior mediastinum with forward displacement of the trachea. The rather full discussion of the microscopic pathology and of the point of origin of these neoplasms is well summarized in the *Conclusions 1:* Small-cell primary tumors of the lungs or bronchi are epithelial in character, as indicated by cell arrangement, relation of connective tissues and blood-vessels, and complete absence of capacity to form reticulum. *2:* Small-cell cancers of the lung originate in the bronchi or bronchioles and are probably unicentric in origin. *3:* Small-cell cancers of the lung more frequently produce large mediastinal masses than do other cancers of this organ and are firmer in consistency, but in other clinical and gross pathological aspects show no distinctive characters.—*Small Cell Carcinomas of the Lung, H. T. Karsner and O. Saphir, Am. J. Path., September, 1930, vi, 553.*—(*R. D.*)

Primary Bronchial Cancer.—The author reports an analysis of the clinical manifestations in 61 cases of primary bronchial carcinoma. In this group were 50 men and 11 women. Only two were under 35 years of age. The onset of symptoms is usually insidious but it may be sudden, with pain in the chest, pulmonary haemorrhage, dyspnoea, or symptoms resembling an acute bronchitis. The relative frequency of the local symptoms in 61 patients was as follows: Cough, 88 per cent; expectoration, 67 per cent; pain

72 per cent; haemoptysis, 45 per cent; dyspnoea, 50 per cent. The cough does not present characteristic features. It usually occurs early, and is not infrequently characterized by periods of improvement and aggravation which are attributed by the patients to attacks of bronchitis. Wheezing is common and has been mistaken for asthma. The expectoration may be absent, scant and mucoid, or profuse and purulent in character. The "currant-jelly sputum" is rarely encountered. Haemoptysis occurred in approximately one-half of the patients. A large fatal haemorrhage is rare. Mild dyspnoea on exertion is common, the more marked forms occurring with bronchial occlusion. Cyanosis parallels the dyspnoea and is explicable by the associated pulmonary complications. Pain in the chest is not only a common but frequently an early complaint of the patient, and tends to become worse as the disease progresses. Fever was present in 55 per cent of the 61 patients at some time while under observation. It is due to associated bronchitis, pulmonary suppuration, bronchiectasis, bronchopneumonia and pleurisy. An early and significant finding clinically is the metastases to the supraclavicular nodes, which, when small, may easily be overlooked. In most instances, extrathoracic metastases are late phenomena. Distinct evidence of metastases to the nervous system was present in 8 cases, and to the abdominal organs in 4 of the group of 61 patients. There may be no abdominal physical observations. Usually, however, the early signs are those of bronchial irritation. Wheezing is common. Unilateral limitation of expansion is the most common sign. In most instances the signs are those of the associated pathological conditions. Bronchoscopy is the only method by which an early diagnosis of bronchial neoplasm can be made with reasonable certainty in the vast majority of patients. Points that are of importance in the differential diagnosis from other conditions are as follows: (Tuberculosis) it is a good rule to question this diagnosis when the sputum contains no tubercle bacilli in the presence of a persisting gross lesion; (Bronchial Obstruction) direct endoscopic examinations should always be made to ascertain the cause, excluding aortic aneurysm before bronchoscopy; (Pulmonary Abscess) generally speaking, a pulmonary abscess of obscure aetiology occurring in a man past 30 or 35 years of age should be suspected as of malignant origin. Quite often differentiation is difficult; (Syphilis) pulmonary syphilis is rare, but may simulate bronchopulmonary new growth. The diagnosis is usually made by exclusion, and the therapeutic test is valuable: (Pleurisy) a pleurisy with effusion may mask the underlying process. In the above series effusion was present in 26.2 per cent, and was haemorrhagic in 10 cases, this finding being suggestive. Among 20 cases coming to autopsy, death occurred within one year in 11 instances, and within 18 months in all but 3 cases. One patient, among those given roentgen therapy, has remained well after six years.—*The Clinical Manifestations of Primary Bronchial Carcinoma, E. H. Funk, J. Am. M. Ass., December 20, 1930, xcv, 1879.*—(*G. L. L.*)

Diagnosis of Cancer of Lung.—Ameuille and Huguenin insist that a direct biopsy is indispensable for diagnosis and that the removal of tissue does not aggravate the disease. Radioscopically, cancer of the lung is often confused with collections of pus. Weill states that the rapid increase in the size of the roentgenographic shadow is a valuable diagnostic criterion. Rist is of the opinion that cancer with cavity-formation is very rare. He also urges frequently repeated X-ray studies. Kindberg cites cases of lung abscess superimposed upon cancer and the primary cause remaining undiagnosed for some time. Biopsy in these cases is necessary. Renaud points out that alveolar pulmonary carcinoma in its early stages progresses very insidiously and bronchial carcinomata give rise to many diagnostic clinical features early in the disease.—*Sur le diagnostic de Cavernes cancéreuses du poumon, Ameuille and Huguenin, meeting Soc. Med. des Hôp., November 29, 1929, reported in Progres Med., December 14, 1929, no. 51, 2207.*—(*U. E. Z.*)

Cancer of Lung Simulating Tuberculosis.—A case is reported of a girl, seventeen years of age, with a history, clinical findings and X-ray apearance pointing to a diagnosis of pulmonary tuberculosis. Later, pressure signs, such as obstruction to the biliary passages, developed. At autopsy, primary carcinoma of the upper and middle lobes of the right lung, with metastases in the mediastinal nodes, pancreas, kidney, ovary, thyroid and lymph nodes along the posterior abdominal wall, were found. There were no signs of tuberculosis with the exception of an old tuberculous pleurisy at the right apex.—*A Pulmonary Neoplasm Simulating Tuberculosis in Adolescence, D. P. Sutherland and J. R. Beal, Tubercle, September, 1930, xi, 529.*—(*M. E. P.*)

Leucin and Tyrosin in Urine in Pulmonary Tumors.—In a number of patients with carcinoma of the lung it was possible to demonstrate leucin and tyrosin in the urine.

The appearance of these amino-acids is dependent on rapid tissue destruction. It was possible, too, to demonstrate these substances in the necrotic part of tumors which stenosed the bronchus. It is concluded that the demonstration of leucin and tyrosin in the urine indicates tissue destruction which may be an important diagnostic indication in those cases in which stenosis prevents the expectoration of sputum.—*Leuzin und Tyrosin im Harn bei Lugengeschwülsten, H. Asperger, Wien. klin. Wchnschr., October 16, 1930, xliii, 1281.*—(*M. P.*)

Lymphogranulomatosis of Lung.—Held recently subdivided the various forms of intrathoracic lymphogranulomatosis into four groups: (1) simple mediastinal lymph-node involvement; (2) mediastinal lymph-node involvement with extension into the lungs; (3) pulmonary involvement independent of mediastinal disease; and (4) disseminated forms. Ten cases of intrathoracic lymphogranulomatosis are briefly reported and 5 roentgenograms are reproduced. The diagnosis of pulmonary lymphogranulomatosis cannot be made from the X-ray film alone since other diseases make similar appearances. Pulmonary cancer with large mediastinal metastases may produce very similar pictures; but the point of differential diagnosis is frequently the fact that in cancer the mediastinal involvement is more likely to be unilateral than in Hodgkin's disease. Concommitant pleural exudates obscure the roentgenological picture and it must be borne in mind that bronchopneumonic and hypostatic foci frequently supervene in the last stages of lymphogranulomatosis. A combination of lymphogranulomatosis and pulmonary tuberculosis is not rare; and such cases present particular diagnostic difficulties. Pulmonary congestion produced by the mediastinal involvement may obscure small parenchymal metastases, and atelectasis may complicate the picture. In rare cases the specific lesions may excavate. In the 10 cases reported the frequency of metastases in bones was striking.—*Über Lungenbefunde bei Lymphogranulomatose, E. Saupe, Klin Wchnschr., August 9, 1930, ix, 1495.*—(*M. P.*)

Tuberculosis and Chronic Arthritis.—The author points to the similarity between chronic articular rheumatism and chronic pulmonary tuberculosis. There exist the necessity for a primary focus, and the existing allergy leading to inflammatory symptoms in articular rheumatism and the parallelism with the perifocal inflammation in chronic pulmonary tuberculosis. New stages follow in both diseases in the form of perifocal inflammation which the new disease adds to the old more or less exhausted inflammatory changes. Likewise, in tertiary pulmonary tuberculosis as in chronic articular rheumatism, the disease develops a relative anergy toward the disease organism localized in a certain organic region. The seasons of winter and spring appear to be the so called critical times which are also associated with a relative vitamine deficiency. It is concluded that the acute exacerbations of both diseases can be prevented by the administration of certain forms of yeast.—*Lungentuberkulose, Gelenkrheumatismus und Präkarenz, L. Heumann, Beitr. z. Klin. d. Tuberk., 1930, lxxiii, 384.*—(*H. J. C.*)

Malaria and Resistance to Tuberculosis.—It has been observed that the tuberculosis mortality in Greece stands in reciprocal relation to the mortality from malaria. Pulmonary tuberculosis in patients with malaria usually runs an afebrile course and is a very fibrotic disease. One hundred and twenty-five patients with acute or chronic malaria were given the Pirquet tuberculin test; 96 reacted. In 18 of the reactors the reaction was much weaker during the febrile attack. In a group of malarial patients with cachexia no reactions occurred. The Pirquet test was positive in 75 per cent of healthy adults in the same locality. Experience with the opsonic index on individuals with and without malaria revealed but little except a tendency for it to be higher in the malarial persons.—*Ueber den Einfluss der Malaria auf den Widerstand des Organismus bei Tuberkulose, K. N. Kyriasidis, Deutsche med. Wchnschr., June 13, 1930, lvi, 995.*—(*H. S. W.*)

Metastatic Abscesses of Brain.—Twenty cases of metastatic abscess of the brain were studied clinically. The diagnosis had been established either by necropsy or surgical exploration. For convenience the cases were classified in three groups. In group 1 were 3 cases in which the abscesses were secondary to an overwhelming or progressive general septic process, in group 2 were 14 cases secondary to pulmonary or pleural suppuration, and in group 3 were 3 cases secondary to an original septic process that had apparently healed but the signs of cerebral suppuration had appeared later and progressed to menace the life of the patient. The prognosis depends entirely on the severity and progress of the original infection. In group 1 the condition was hopeless. In group 2 it was grave, but in some of the cases it might have been modified by operation. In group 3 surgical treatment at a favorable time was possible and the outcome favorable. The course of metastatic ab-

scesses of pleural or pulmonary origin was much shorter than that of abscesses due to other causes. This no doubt depended largely on the debility of the patient. The clinical signs and symptoms, however, differed little. The severity of the original infection added a complicating feature, often making the diagnosis extremely difficult. In 10 of the 20 cases a single abscess was situated in one or the other lobe of the cerebrum. In many of these a certain degree of encapsulation was present but rupture into the ventricle nevertheless occurred readily. In the other 10 cases the brain was the seat of multiple foci of suppuration.—*Metastatic Abscesses of the Brain. A Clinical Study, H. L. Parker, Am. J. M. Sc., November, 1930, lcxxx, 699.*—(*W. I. W.*)

Red-Cell Sedimentation and Leucocytes in Prognosis of Tuberculosis.—The blood picture and sedimentation rate are valuable in determining the prognosis in pulmonary tuberculosis. In most cases there is an agreement between these two features and the clinical condition, but in individual cases the blood picture and sedimentation rate run divergently. Among 369 patients there were 82, or 22 per cent, with divergent findings, and, after excluding cases with complications or too short an observation period, there remained 41 which could be used for comparison. In these there was a marked advantage in the leucocytic formula over the sedimentation rate, in that 37 of the cases paralleled the clinical course, while in only 4 was the sedimentation rate in agreement. It is concluded that the haemogram is more rapidly influenced by the immunobiological state than the sedimentation test.—*Blutkörperschensenkung und weisses Blutbild in der Prognose der Lungentuberkulose, H. Vos, Zeitschr. f. Tuberk., 1930, lv, 431.*—(*H. J. C.*)

Value of Pirquet Reaction in Prognosis of Tuberculosis.—The Pirquet reaction was found to be of no prognostic significance in pulmonary tuberculosis since even bleb formation was found as frequently in severe cases as in mild ones. A study of the negative anergic condition in cases of pulmonary tuberculosis gave no new information.—*Der Wert der v. Pirquetschen Reaktion für die Prognose der Lungentuberkulose, M. W. Marman, Zeitschr f. Tuberk., 1930, lv, 400.*—(*H. J. C.*)

Tuberculosis Mortality.—The Health Section of the League of Nations has given a comprehensive statistical review of the mortality from tuberculosis in various countries during the last fifty to eighty years. Figures have been collected and arranged to facilitate the testing of current theories relating to the epidemiology of this disease. There have thus been brought to light notable changes in the mortality rates, and the existence of definite trends in that mortality as regards the populations of cities and rural areas, and at various age-periods in both sexes. It is impossible to accept all the mortality figures, as some are grossly deceptive and practically all are inaccurate, though in varying degrees in different countries. It is clear that the age-distribution of tuberculosis has distinctly altered during the last fifty years in many civilized countries, and that the relative incidence of the various clinical symptoms has also changed. Morbidity has declined less than mortality, except in primitive and agricultural countries, where tuberculosis is still advancing, and where the ratio of illness to mortality is lower than in urbanized countries. Mortality from tuberculosis has diminished in practically all countries for which statistical data are available. The excess of male mortality is larger in the cities than in the various countries taken as wholes; it is more pronounced in the great cities, and lower or nonexistent in the smaller towns. In rural districts there may even be an excess in the female rate. There is no clear-cut correlation between industrial employment and the excess of male mortality. In all countries and periods the highest mortality occurs in the first year of life. The curve then falls rapidly, reaching its lowest point between the ages of five and fifteen years, and increasing rather abruptly from fifteen to twenty-five years. After this, it either remains high or decreases according to the type of community, the country and the period. When a generation is highly infected with tuberculosis in infancy, it presents a persistently high death-rate through the normal span of life. A period of high infant tuberculosis mortality is followed after about twenty-five years by a high death-rate of young adults, and of mature adults some twenty-five years later again, an interval of some sixty to seventy years elapsing between the waves of high mortality in infants and in old people. A generation of young parents with a high tuberculosis morbidity will in turn give rise to a new generation of infants similarly infected, and so the type of curve will persist, unless new factors supervene to diminish the mortality at one point or another, when the curve will change correspondingly.—*Mortality from Tuberculosis: Report by the Health Section of the League of Nations, Brit. M. J., June 27, 1931, no. 3677, 1127.*—(*M. E. P.*)

Epidemiology of Tuberculosis of Negroes.—Of ten million colored people in the

United States, approximately twenty-five thousand die every year from tuberculosis. Knowledge of those peculiar characteristics of the disease in the negro that explain this appalling mortality is astonishingly defective. It is not definitely known if the tuberculosis of the American negro produces pathological changes that in part distinguish it from the tuberculosis of white people living in close proximity to them. Little is known concerning the morbidity as distinguished from mortality. Almost nothing is known concerning the prevalence of minor infections which are often the precursors of fatal disease. No effort has been made to determine how tuberculosis spreads among colored people or what are the peculiar conditions that modify this spread. Better knowledge concerning these very practical questions offers the best promise of improved measures for control of the disease. For colored people the mortality from tuberculosis in both men and women reaches a maximum between the ages of twenty and twenty-four years, when it is four times that of white people. The disease begins in adolescence or early adult life and pursues a rapidly fatal course. In white people it pursues a more chronic course and tends to cause death at a later period of life. The appearance and spread of tuberculosis among the native population of Africa and Jamaica demonstrate the susceptibility and rapidly fatal course of tuberculosis among the black race. Autopsies demonstrate that the lesions usually resemble those of children in this country. It has the familiar aspects of a first infection, with subapical lesions, massive enlargement and caseation of adjacent tracheobronchial lymph nodes. There may be an intimate relation between tuberculosis in the negro and his environment. Tuberculosis is primarily a disease of poverty and the economic conditions under which many colored people live are such as favor the spread of the disease.—*The Epidemiology of Tuberculosis of Negroes, E. L. Opie, Tubercle, February, 1931, xii, 207.*—(*M. E. P.*)

Tuberculosis in India.—Tuberculosis, while prevalent in most Indian cities from ancient times, has rapidly increased within recent years. There has been a rise of 70 per cent in the mortality rate from tuberculosis within the last ten years in Calcutta. The course of the disease seems to be more acute than in western countries. Ninety per cent of the population reside in villages. Urbanization, modern industrialism, and the introduction of rapid-transport facilities have been powerful factors in the diffusion of the population. Unhygienic habits favor massive infection. Unbalanced and inadequate diets favor malnutrition. Bovine infection is practically nonexistent. The mortality rate in the earlier years of life is low, reaching 4 per cent by the fifteenth year. It rises rapidly to its peak at thirty years, then it falls slowly to 7 per cent by the sixtieth year. Ninety-four per cent of deaths from tuberculosis in Calcutta are from the pulmonary form. Of 6,500 individuals tested for tuberculosis by the Pirquet method, 45.9 per cent were positive. This figure is far below those of European countries. In a series of 52,550 patients attending the Polyclinic of the Calcutta hospital, the following incidence of tuberculosis was found: Total number of tuberculous cases, 1,019. Of these the lungs were affected in 62.8 per cent; lymph nodes, 17 per cent; bones and joints, 13.9 per cent; while skin tuberculosis accounted for only two in the series. Pulmonary tuberculosis was extremely rare below ten years of age. All forms of tuberculosis attained their maximum incidence between twenty-five and thirty years, five to ten years earlier than those found in Europe. The duration of life of a case of pulmonary tuberculosis, which depends on the infecting dose, the age, the extent and multiplicity of lesions, the secondary bacterial flora in open cases, and on the immunity of the individual, is distinctly shorter in India than in Europe. It is shorter in females than in males. Pregnancy, lactation, diabetes, influenza and kala-azar shorten the course. Massive infection is the rule in a majority of cases. Postmortem evidence, based on 1,000 consecutive necropsies in Calcutta hospitals, shows the prevailing type of pulmonary tuberculosis to be the fibrocaseous form, with primary localization in one lobe and rapid spread to other parts. Only 10 per cent of cavities show well developed fibrous tissue in the walls. Exudative changes are more prominent than proliferative processes. Lesions of the peritoneum, pericardium, spleen and liver are more common in Calcutta, whereas laryngeal involvement is more frequent in London. The explanation of massive infection on an imperfectly immunized soil interprets most of the lesions found in India. The major part of the population possess a degree of specific resistance to tuberculosis intermediate between that of primitive African and the well-immunized European races. After a long series of experiments, it is believed that the secondary bacterial flora is richer and more varied in India than in Europe, and that, apart from the ulcerative processes, it either augments the virulence of the tubercle bacilli, or aids the growth and multiplication of them. Metabolic factors, such as calcium content

of soils and water, and the calcium and cholesterol content in blood, do not differ very much from European data, and do not seem to play a large part in the process. Hot weather and monsoon winds, however, affect tuberculosis patients unfavorably. The influence of sunlight seems to play an important part in limiting certain types of tuberculosis, such as lupus and bovine infections.—*A Note on the Epidemiology and Pathology of Tuberculosis in India, A. C. Ukil, Tubercle, March, 1931, xii, 244.*—(*M. E. P.*)

Conjugal Tuberculosis.—A detailed study of the cases in which pulmonary tuberculosis existed in both husband and wife, and of those among widowed patients whose husbands or wives suffered similarly, failed to produce any evidence of unduly high infection of husband by wife or *vice versa.*—*A Survey of Some Findings in Five Years' Work on Tuberculosis, J. A. Struthers, Tubercle, December, 1930, xii, 99.*—(*M. E. P.*)

Domiciliary Tuberculosis Contacts.—The incidence of tuberculous infection in sputum-positive households in Worcestershire has been studied. Sufficient evidence is produced to establish the fact that house contacts of sputum-positive cases of tuberculosis suffer both an incidence rate of, and a death-rate from, tuberculosis, very significantly greater at all ages than the corresponding rate for the general population. It is emphasized that all contacts of sputum-positive cases are themselves potential cases of tuberculosis and they should be periodically examined and preventive treatment instituted before the contact has reached the stage of being "notifiable" according to the generally accepted standards.—*The Actual Tuberculous Morbidity and Mortality among House Contacts of Sputum-Positive Cases in North Worcestershire, H. M. Turner, Tubercle, January, 1931, xii, 146.*—(*M. E. P.*)

Pulmonary Tuberculosis in Childhood.—The term, "childhood type" of tuberculosis, refers to lesions in the lungs and intrathoracic lymph nodes which result from first infection with the tubercle bacillus. It is generally accepted that pulmonary tuberculosis occurring during the first year of a child's life tends to progress rapidly, and to cause death from acute general tuberculosis or tuberculous meningitis. In the second year there is still little or no tendency to healing, and death usually takes place. After this period and until the age of about ten years, acutely progressive and rapidly fatal tuberculosis of the lungs becomes less common. Pulmonary tuberculosis in the child has certain definite characteristics. An area of inflammation develops where the bacilli settle in the lung, which may be small, or large enough to affect an entire lobe; from it the regional mediastinal lymph nodes are quickly involved and become enlarged. The parenchymatous lesions may heal and almost entirely disappear, a small area of calcification, that is, Ghon's focus, being left. In a comparatively short time the lymph nodes may show calcific deposits or they may remain caseous. The parenchymatous lesion may be localized in any part of the lung, least frequently in the upper lobes, and, after the subsidence of the initial inflammatory changes, may be difficult of demonstration radiographically. Caseous lesions tend to become calcified and cavitation is rarer than in the adult type. The distribution of the disease conforms most usually to one of three types; namely, a diffuse miliary form, a localized form in which the lesion may be large or small and represented by a caseous mass with a fibrous periphery or by a massive lobar infiltration, or a bronchopneumonic distribution. In many cases physical examination alone gives insufficient evidence upon which to base a diagnosis. Exposure to tuberculosis within the family is important, and a history of attacks of phlyctenular conjunctivitis, or erythema nodosum, or of pleurisy is suggestive of tuberculous infection. Symptoms may be absent. When they exist they may vary in intensity from those associated with a so called cold to those accompanying a pneumonia. The following factors are important in making a diagnosis: (1) the presence of physical signs and symptoms; (2) definite involvement of the parenchyma, hilum, or both, as revealed by X-ray; (3) a positive reaction to a tuberculin test; (4) the demonstration of tubercle bacilli; and (5) a history of exposure within the family. A positive tuberculin test and X-ray examination, when other causes for the condition in the lung have been ruled out, may be accepted as sufficient for a positive diagnosis in many cases. Children with active disease should be given prolonged periods of treatment in a sanatorium. Children with latent tuberculosis, and those who give a positive reaction to the tuberculin test should be kept under supervision for prolonged periods.—*Pulmonary Tuberculosis in Childhood, G. B. Dixon, Brit. M. J., April 25, 1931, no. 3668, 694.*—(*M. E. P.*)

Tuberculization and Tuberculosis in Children.—In a survey of the histories of 453 children examined for tuberculosis in urban dispensaries, the following conclusions

were drawn relative to the tuberculin test, tuberculization and tuberculosis in relation to age and contacts. It was found that the tuberculin test is usually positive in those bodies harboring live tubercle bacilli. Anergic states are an exception to this rule. With this exception, a negative reaction is a satisfactory indication that the body does not harbor live bacilli. The Pirquet method appears satisfactory during the early years of life but its significance in relation to disease varies with age. In infants sensitivity is high and resistance to disease relatively low, so that infection in the first four years of life is dangerous. Childhood is a period of relatively low sensitivity, high tolerance and relative latency of disease. At adolesence, social, physiological and economic changes undermine the general health. Sensitivity tends to rise and resistance to fall. Although previous infection still offers protection to some, in others old lesions are prone to reactivation. Fresh infection is dangerous. Disease is more common in female contacts than in males. Contacts remaining healthy during childhood show a high incidence of tuberculosis during adolesence. Recrudescence in those previously diseased is also common during adolescence. Contact examination must include the following up of cases, especially during adolescence.—*Tuberculization and Tuberculosis in Children under Urban Conditions: with Special Reference to "Contacts," R. J. Matthews, Tubercle, February, 1931, xii, 193.*—(*M. E. P.*)

Leucocytes in Tuberculosis of Infancy and Childhood.—This study of 68 infants and children, ranging in age from 5 months to 12½ years, was undertaken to compare the clinical and pathological course of tuberculosis with the blood findings, especially as regards the differential white blood cell picture determined by supravital staining (Cunningham, Sabin, *et al.*; Blackfan and Diamond) and in some instances by fixed smears (Flinn and Flinn, Medlar, and others). The findings may be tabulated as follows: *Group 1*: 12 cases of severe pulmonary and mediastinal tuberculosis, including 6 with tuberculous meningitis and 2 with tuberculous peritonitis. There were an increase in the total leucocyte count, an increase in polymorphonuclear cells and monocytes, a decrease in the total lymphocyte count, and a high monocyte-lymphocyte ratio as compared with the "normal" given by Blackfan and Diamond for various ages. *Group 2*: 5 cases considered active lymphatic tuberculosis. In these there was a leucopoenia, with the M:L ratio as a rule above normal. In 2 this was due chiefly to an increase in the total monocyte count and in 3 chiefly to a decrease in the total lymphocyte count. Two of the latter, in whom the marked decrease of lymphocytes and increase in M:L ratio suggested severe tuberculosis, died of extension of the process, although during the course of the counts the lesion was considered roentgenologically and clinically limited to the hila. *Group 3*: 5 cases with multiple lesions of long duration showing evidence of clinical improvement, and *group 4*: 6 cases including epituberculosis erythema nodosum, and phlyctenular disease, showed no characteristic changes in the cases as groups, although in group 4 there was a wide fluctuation in the counts, considered as possibly due to the fluctuations in the amounts of tuberculin products responsible for the local specific tissue reactions. *Group 5*: 11 cases of advanced healing or healed tuberculous lesions. Leucopoenia was the rule, with normal or decreased M:L ratios and, except in 3 cases, increased total lymphocyte count. In these three cases the multiple lesions, although clinically healing, were extensive. *Group 6*: 9 cases with variable clinical symptoms and complicated pathological processes. No consistent conclusions could be drawn from the group as a whole. *Group 7*: 3 cases with ulcerative Pirquet reactions, but no definite clinical or roentgen evidence of tuberculosis. There were no constant blood changes warranting in themselves a diagnosis of tuberculosis. *Group 8*: 7 cases of various diseases with negative tuberculin tests and no clinical or roentgen evidence of tuberculosis but with blood findings (modified monocytes and increased M:L ratios) theoretically indicative of tuberculosis. In one case of bleeding duodenal ulcer and marked secondary anaemia, the large number of modified monocytes was interpreted as a result of the regenerative bone-marrow activity. *Group 9*: 10 cases with a variety of nontuberculous diseases and no blood findings indicative of tuberculosis. From these studies it may be concluded that in active tuberculosis there is an increase in total monocytes, a decrease in total lymphocytes, and an increase in the M:L ratio, the extent of these changes varying with severity of the disease. As healing occurs, the M:L ratio decreases, with fluctuations until the healing is well advanced. The changes in the lymphocyte count are more constant than in the monocyte. The great value of the white blood cell picture in tuberculosis in children lies in the distinction between active severe tuberculosis or an early healing tuberculosis and an advanced healing or latent tuberculosis in the child who shows some of the clinical signs of tuberculosis but no definite

symptoms by which to determine the status of the pathological process. A reliable fixed-smear method will supply the necessary information regarding the total number of lymphocytes and monocytes.—*Tuberculosis in Infants and in Children: White Blood Cell Counts; Evaluation of the Monocyte-Lymphocyte Ratio by the Supravital Staining Method, B. M. Hamil, Am. J. Dis. Child., May, 1931, xli, 1023.*—(*M.D.*)

Prevention of Tuberculosis.—The program mapped out for preventing tuberculosis is based upon the tenet that, except in the relatively small percentage of cases suffering from tuberculosis of bovine origin, most of the patients had acquired the disease through contacts with preëxisting cases in their homes. The three chief lines of attack are (1) removal of infected persons from their homes, (2) removal of susceptible persons from infected homes and (3) protection of those exposed to home infection from the risk of developing tuberculosis. The first of these has been the most fruitful of results. With earlier and more accurate diagnoses and with more coöperation of the general practitioners and health officers, the efficiency of this mode of attack will be brought to a still higher level. With regard to the second plan, the removal of susceptible persons may be temporary or permanent. Temporary removal should be made to preventoria, open-air schools, hospitals and sanatoria, etc., but the institution should not carry a name suggestive of tuberculosis because of the stigma associated with consumption. The third plan, namely, that of protecting the family which harbors an infectious person, aims at building up resistance through extra nourishment, making periodical complete check-ups, including X-ray examinations, and instructing the parents and children regarding the risks incurred. While tuberculosis of bovine origin is relatively unimportant as a cause of death in man, it can be stamped out by the simple process of pasteurization of milk.—*The Prevention of Tuberculosis, S. L. Cummins, J. State Med., February, 1931, xxxix, 83.*—(*J. P. B.*)

Prevention of Tuberculosis in Children.—In seeking the most practical attack on infant and adolescent mortality due to tuberculosis, a most rewarding procedure is to be found in the serial examination of those living in household contact with sputum-positive tuberculosis. In a report based on observations extending over slightly more than two years, it is shown that among a group of children of whom either the father or mother had positive sputum, about 9 per cent showed clinical tuberculosis, about 2 per cent well-defined latent pulmonary infiltrations, and about 20 per cent calcification of the tracheobronchial lymph nodes. In these children the number of pulmonary lesions has increased during four years of subsequent observation. The immediate problem of supervision is the severity and length of infection to which any infant has been exposed. Even a weak tuberculin reaction may signalize a dangerous infection in an infant. Every precaution should be taken to prevent reinfection and to maintain the child in the best possible living conditions. Annual X-ray examinations should be the rule for a seven-year period after contact. They afford basic information about the state and possibilities of a lesion even when physical findings and blood pictures are negative. Economically, the greatest waste in the supervision of tuberculosis arises from the failure to institute prompt and proper treatment.—*Some Aspects of Prevention of Tuberculosis in Children, F. M. McPhedran, Brit. M. J., February 28, 1931, no. 3660, 342.*—(*M.. E. P.*)

Open-Air Schools.—The first authentic open-air school was established in the Grünewald, near Charlottenburg, Berlin. It was a convalescent home with some educational purpose. Before long the idea had spread to Great Britain, where the first similar institution was opened about 1900. There are now about 110 open-air schools in England and Wales. Less than 8,000 places are available in these, while the elementary school enrollment is five and a half million. This inadequate provision may be attributed in part to indifference but is due also to increased costs. The initial construction is estimated at a slightly higher figure than for the ordinary elementary school while the cost of maintenance is estimated at about $160 per child per year in comparison to $65 in the ordinary school. The fact is overlooked that many of these children would have to be provided for somewhere in any event, and that the gain to the community in preventing infection from developing into clinical disease is incalculable. The cases which should have the advantage of open-air schools include (1) those with malnutrition, rickets or anaemia; (2) delicate children living in a house with a consumptive; (3) children with tuberculous cervical lymph nodes; (4) convalescents from debilitating diseases such as pneumonia, measles and whooping-cough; (5) convalescents after operations for adenoids, cervical lymphadenitis, etc.; (6) blepharitis and chronic diseases of the eye associated with malnutrition; (7) certain types of crippled children; (8) nerv-

ous and highly strung children; and (9) myopes. The open-air regimen of the school stimulates the appetite, and most schools provide one or two meals and a glass of milk between meals. A period of rest in the recumbent position in the open air is provided. No conversation is allowed, and often the children will sleep. The gain in weight is usually striking and the increase in haemoglobin often exceeds 10 per cent. On the educational side it has been estimated at Nottingham that a scholastic advance of 17.4 months was made in 12 months. Although less time is spent on the purely mental side, the mind is better able to grasp the material presented. From the standpoint of a worker in tuberculosis, it seems important that the preventive possibilities of these schools should be recognized, and that open-air schools should be considered, not merely as clinics for the few pronounced cases of active disease, but a nursery of protective influences for the whole school population.—*Education and the Physiological Life: the Open Air School, H. Williams, Brit. J. Tuberc., April, 1931, xxv, 80.*—(*R. D.*)

Protection of Pupils from Tuberculous Teachers.—Teachers may propagate tuberculosis in schools. It is important that they be examined before they enter such an occupation. Teachers, pupils and other persons in school who suffer from active pulmonary tuberculosis are to be excluded from school attendance. Periodic examinations of teachers are essential. These are advisory directions supplementing a general health bulletin of 1929.—*Reichsgesundheitsrat und Lehrertuberkulose, Paetsch, Deutsche med. Wchnschr., October 17, 1930, lvi, 1787.*—(*H. S. W.*)

Protective Inoculation against Tuberculosis.—Independent of Calmette, Uhlenhuth has made use of prophylactic vaccination in calves by administering attenuated bovine tubercle bacilli. This work has gone on for twelve years. The attenuated strain was a twenty-year-old culture, which originally (1902) was virulent for guinea pigs and calves but by 1921 and 1923 had lost much of its virulence, so that calves could tolerate 100 mgm. intravenously. In 1926 and 1927 six calves, six months old, were vaccinated intraperitoneally with 1 gm. of this culture, and put together under natural conditions in a stable with 5 unvaccinated control animals and with one or two tuberculous calves with open disease. After ten months, only one of the vaccinated animals remained healthy; the other five were tuberculous. Calmette's communications are surprising because he obtained in calves an effective immunity with an avirulent culture of bovine tubercle bacilli. Next, *BCG* and the strain just described were put to test as to their immunizing effect on calves. Six animals received 100 mgm. of Calmette's culture subcutaneously and six the same dose of the author's culture (Tb18) subcutaneously. Six were also given 1 gm. of Tb18 intraperitoneally and six served as controls. The animals were isolated for three months and then were put together in a stable with 3 animals having open tuberculosis. At autopsy ten months later two of the 6 *BCG* animals were free from tuberculosis and two from each of the lots that had been treated with Tb18 were likewise free. All others, including the controls, showed progressive tuberculosis. The animals vaccinated with Calmette's culture were as much or as little protected against natural stable infection as those vaccinated with the Tb18 strain. The result of the vaccination would undoubtedly be better if the vaccinated animals were to be placed in a large herd where there would be few or no cases of open disease. None but experiments which last for years can decide the value of Calmette's vaccination in calves, because in the natural state the conditions of infection are very complex. The proposition of Calmette to vaccinate newborn calves may improve the degree of protection as may also repeated vaccinations and larger doses. So far the experiments reported were, at most, specific for a certain degree of immunity which is of short duration. One should take a watchful attitude, at least as to the protective vaccination of human beings. Isolation of children and general hygienic measures remain matters of greatest importance.—*Zur Frage der Schutzimofung gegen Tuberkulose, Uhlenhuth, Deutsche med. Wchnschr., October 17, 1930, lvi, 1769.*—(*H. S. W.*)

Remarks on *BCG*.—There is beginning to creep into the German literature some doubt as to the efficacy of *BCG* as a protective manoeuvre against tuberculosis. Its innocuousness for animals and human beings is unquestioned. Calmette believes that he has statistically demonstrated a retrogression of the mortality from tuberculosis in children since the introduction of his vaccine. Strangely, also, he claims a decrease of general child mortality by this vaccination of 40 to 50 per cent. A statistical study of tuberculosis mortality and general mortality of children and adults in the state of Baden has been made. In the year 1929, 82 children died of tuberculosis in a population of 2,500,000. In 100 deaths of children

of all causes, there were only 1.9 per cent from tuberculosis. From 1924, when Calmette first began his protective inoculation, to 1929, the tuberculosis mortality fell in this state (Baden) from 8 per 10,000 children to 3.5 per 10,000 children; that is, approximately 55 per cent or in about the same degree as Calmette claimed for his vaccinated children. There has been a more favorable retrogression of the mortality rate in tuberculous children than in tuberculous adults. In 1900, for instance, there died in Baden of tuberculosis 26.8 children per 10,000 living and in 1929 only 3.5 per 10,000, whereas the mortality of young adults (15 to 30) in the same locality fell from 32.8 to 11.1 and of adults over 30 it fell from 31.9 to 12. In 29 years the death-rate from tuberculosis in infants fell eight to one without vaccination but under the guidance of a modern official health-service. The fight against tuberculosis in young adults from 15 to 30 is more important, as in this period tuberculosis is still the cause of approximately 35 per cent of all deaths. Here, artificial and natural vaccination fail and only the increase of natural resistance brings about a change. Calmette's objection that the general mortality of vaccinated children is lower than that in the nonvaccinated rests probably on the fact that parents who bring their children to the tuberculosis health officer are parents who in other respects take better care of their children, be it in nutrition, dwelling-place, general cleanliness, etc., and it is this higher standard of living which is responsible for the decrease of tuberculosis in his data.—*Die Tuberkuloseschutzimpfung von Calmette, Berghaus, Deutsche med. Wchnschr., October 17, 1930, lvi, 1771.*—(*H. S. W.*)

Studies on *BCG*.—The pathogenicity of *BCG* depends very largely upon environment. When grown on a bile-glycerine-potato medium it is relatively innocuous, even in large doses. When its environment is changed to a Sauton-normal-rabbit-serum medium and the organism continuously cultured on this medium for a short period it becomes very virulent. This work substantiates the observations of Petroff and Branch on the "dissociation" of *BCG*. The virulent culture is smooth, veil-like, colorless, and is easily emulsified. The culture of low virulence is rough, compact, often chromogenic, and is emulsified with difficulty. Since it is possible to bring about such a marked alteration of *BCG in vitro*, and since so little is known relative to the factors that enhance or retard the pathogenicity of the tubercle bacillus, it would seem essential to use great caution in any application of *BCG* as a prophylactic vaccine against tuberculosis.—*Studies of the Bacillus-Calmette-Guérin Strain of the Tubercle Bacillus, K. T. Sasano and E. M. Medlar, Tubercle, February 1931, xii, 214.*—(*M. E. P.*)

Lübeck Disaster with *BCG*.—In the early part of 1930, there occurred at Lübeck in Germany a disaster accompanying the use of prophylactic vaccines. The vaccine used was prepared from the *BCG* strain of tubercle bacillus, which, as the result of subculture for several years on a glycerin bile-potato medium, had become almost entirely avirulent to man and animals. During a period of two months, from February 24 to April 25, 1930, this vaccine was administered to 249 newly born infants. Of these, many developed acute tuberculosis during the next few weeks and died; others developed subacute lesions, while a considerable proportion remained perfectly well. The total death-roll up to January 29, 1931 was seventy-five. On July 28, 1929, a strain of *BCG* was sent from the Pasteur Institute in Paris to Professor Deycke of the General Hospital in Lübeck. Some time after its arrival, the culture was inoculated into animals, and proved to be apparently avirulent. According to Calmette the same strain was also sent to Mexico and to Riga, and the following subculture was used for the preparation at the Pasteur Institute of a vaccine which was administered to 3,015 infants without any detrimental results. There is therefore very little doubt that the culture originally sent from Paris was avirulent. Although it has been Calmette's practice to keep the *BCG* strain on a glycerin-bile-potato medium, and for the preparation of vaccine to grow it in Sauton's liquid medium, Deycke subcultured his strain on egg medium, and used these solid cultures for the subsequent preparation of his vaccine. For a time, the *BCG* strain was the only culture of tubercle bacilli in the laboratory, and it was kept in a small room. Later another strain was sent to the laboratory, but it was kept in a large room. On December 9, 1929, a preliminary inoculation was made of one child, which had been removed at birth from a mother suffering from open tuberculosis. A second child was vaccinated on December 30, 1929. The first child developed cervical lymphadenitis which was attributed to congenital infection. The second child remained well, but developed a positive tuberculin reaction. One further preliminary inoculation was made on February 10; this child subsequently developed mild symptoms of tuberculosis. Then the main series of vaccinations was

commenced on February 28, and about 50 per cent of those born in Lübeck up to April 28 were inoculated, the usual three doses being given in the first ten days of life. Although suspicions were early aroused by the clinical condition of the vaccinated infants, nothing definite occurred until April 17, when a child, vaccinated thirty-three days previously, died. On April 20, a second child died, and was found to have generalized tuberculosis. Since the lesions were most marked in the lungs, it was concluded that the child had been infected by the respiratory tract from its mother. It was not until the third and fourth children died, on April 25 and 26, that the pathogenic nature of the vaccine was fully realized, and further distribution stopped. At this juncture, Professor Deycke, in order to avoid any possible error, destroyed all the remaining vaccine in the laboratory, together with the existing subcultures of the *BCG* strain. This unfortunate step, which was clearly open to more than one interpretation, added greatly to the difficulties of the subsequent investigation. The real point at issue is whether another strain of tubercle bacillus became mixed with, or substituted for, the *BCG* strain in the preparation of the vaccine, or whether the *BCG* strain actually underwent a spontaneous increase in virulence. It is impossible to decide which of the two hypotheses is correct. In the absence of definite evidence it is wise, though unsatisfying, to maintain an open mind as to the real cause of the catastrophe. The moral, however, is plain. The preparation of vaccines for large-scale distribution should be undertaken only under the most rigidly controlled conditions in laboratories set aside for this and for no other purpose.—*The Lübeck Catastrophe; a General Review, Editorial, Brit. M. J., June 6, 1931, no. 3674, 986.*—(*M. E. P.*)

Lübeck Disaster with *BCG*.—Bruno Lange controlled tests which showed definitely that the material for vaccination in Lübeck comprised cultures that were partly pathogenic and partly nonpathogenic for guinea pigs. The Ministry of Health cultured virulent and nonvirulent tubercle bacilli from residual vaccination material. Cultures of organs of infants who had died from the inoculation showed likewise the virulent and nonvirulent bacilli. Some of these cultures, when injected into guinea pigs, led to generalized tuberculosis, and some led to a retrogressive disease of the lymph nodes, which when the animals were killed after three months proved to be tubercle-free. It would appear that by mistake a weakly virulent strain of tubercle bacillus had been mixed with the *BCG* cultures and thus led to the disaster. However, there is still the possibility of a change of the *BCG* bacillus back to its original virulence. The claims of Petroff and Watson in increasing the virulence of *BCG* or in causing its dissociation into a virulent and avirulent strain are doubted. The change of nonvirulent to virulent cultures has apparently been shown in certain bacteria. To get a clear conception of the value and harmlessness of *BCG*, long-continued observations of vaccinated children are necessary.—*Die Todesfälle in Lübeck und der augenblickliche Stand der Calmette-Frage, F. Neufeld, Deutsche med. Wchnschr., November 28, 1930, lvi, 2056.*—(*H. S. W.*)

Tuberculous Meningitis in *BCG* Subject.—An infant was vaccinated with *BCG* on the 3rd, 5th, and 7th days of life. At 26 months it weighed 9,100 gm. and until that time was in good health and developed normally. Until the age of 16 months there was no known exposure to tuberculosis. During the following three months, however, the child was exposed to a step-brother who died six months later of pulmonary tuberculosis. At the age of 26 months the child developed sleeplessness which was attributed to teething. Two days later it began to have an irregular fever, in a few days developed meningitic signs, and died fifteen days after the onset of symptoms. Spinal fluid three days before death contained low sugar, 40 cells per cmm. (40 per cent lymphocytes), and acid-fast bacilli on smears, with a negative Wassermann. The cutaneous tuberculin reaction two days before death was negative. It is advisable to record cases of this nature, although no conclusion is drawn.—*Mort par meningite tuberculeuse d'une enfant de 2 ans vaccinée par le BCG, G. Blechman et A.-E. Levy, Nourrisson, March, 1931, xix, 110.*—(*M. D.*)

Fatal Tuberculosis in *BCG* Subject.—A poorly nourished, underfed, rachitic infant with pyodermia, whose mother had died in childbirth and who had been boarded out under poor conditions, was admitted at the age of 13 months. The intracutaneous tuberculin test (1:1,000) was negative 40, 75 and 90 days, respectively, after admission. Physical examination of the lungs was negative except on one occasion, 80 days after admission, at which time subcrepitant râles were heard at both bases. On the 92nd day 1/80 mgm. of *BCG* was given subcutaneously without local or general reaction. In the course of the next four months, the child developed progressive cachexia, fever, and signs of cavitation in

the left upper lobe, accompanied by X-ray evidences of extensive pulmonary tuberculosis (primary complex of infancy) with a terminal acute miliary tuberculosis. An analysis of the possibilities as to the course of events suggested as the most logical explanation that the child had a low-grade tuberculous infection on admission, unaccompanied by skin allergy, and that the rapid development of the lesion following subcutaneous administration of *BCG* was due to the focal lighting up of the process, a possibility that has been noted by Weill-Hallé.—*Un cas de tuberculose mortelle chez un vacciné avec le BCG sous-cutané, E. Jaso, Arch. Med. Enf., March, 1931, xxxiv, 169.*—(*M. D.*)

***BCG* in Vaccination of Calves.**—The claims put forward by Calmette and Guérin have evoked a widespread interest in *BCG*. The literature indicates that the general consensus of opinion in Europe tends to support Calmette and Guérin, whereas in America several workers have not only failed to substantiate their conclusions, but have made definite pronouncements against their methods. It was not maintained even by the originators of *BCG* that the organism is incapable of producing lesions in the animal body, but it is claimed that such lesions are entirely benign and incapable of developing into active foci of tuberculosis. The appraisement of the efficacy and duration of immunity following *BCG* vaccination has led to much discussion and the problem cannot be regarded as solved. The preliminary experiments of Calmette and Guérin on young calves indicated that after vaccination these animals possessed a solid immuity against a test dose of virulent organisms. Subsequent experiments on smaller animals have shown that it is necessary to recognize a distinction between experiments in laboratory animals and those in the bovine species. It seems to be clear that in rodents the immunity persists for a few weeks at most. Some observers doubt whether *BCG* offers any protection to these animals. Two preliminary experiments performed by one of the authors (A.S.G.) with *BCG* and with attenuated human tubercle bacilli showed that the resistance of a calf could be raised to such a degree as to enable it to resist completely the intravenous inoculation of 1 mgm. of virulent bovine tubercle bacilli. The following experiments were undertaken in order to ascertain whether or not vaccination with *BCG* can be relied upon to raise the resistance of calves to tuberculosis and the best method to employ. At first an attempt was made to obtain calves a few days old from herds supposed to be free from tuberculosis. This was found to be impracticable for several reasons, and later animals were purchased from various sources, kept for several weeks, and before vaccination submitted to the double intracutaneous test. Cultures of *BCG* were grown on coagulated 5 per cent glycerinated egg and used when they were from 3 to 7 days old. A convenient amount of culture was weighed and thoroughly ground between sterile glass plates with 2 or 3 drops of sterile salt solution; a thick, smooth, creamy paste was thus produced, which was thinned by the gradual addition of salt solution. Fifty-one calves were vaccinated with *BCG* by various methods: 10 by feeding, 4 intratracheally, 3 subcutaneously, and 34 intravenously. They were subsequently tested as to their resistance to tuberculosis, together with 14 untreated calves, by the intravenous injection of fully virulent bovine tubercle bacilli in doses ranging from 1.0 to 0.25 mgm. of culture. Five control calves received 1.0 mgm. of bovine tubercle bacilli and died in from fifteen and a half to twenty-seven days. Seven calves each received 0.25 mgm. and died in from eighteen and a half to twenty-seven days of general miliary tuberculosis. Two calves were inoculated with 0.1 mgm. and 0.05 mgm. respectively and died in thirty-nine and sixty days. The vaccine was administered to six calves by pipette into the mouth in doses ranging from 0.5 to 2.1 gm. Three of the calves showed no higher resistance than the controls, while the other three showed much higher resistance, amounting in one instance apparently to complete immunity. Four calves were fed with *BCG* in the milk. The resistance of two of these calves was a little higher than that of the controls while that of the remaining two was much higher. Three calves were vaccinated by subcutaneous inoculation. One showed little, if any, increased resistance, and one showed slightly increased resistance. The remaining one exhibited a moderately high resistance. Four calves received directly into the trachea doses of *BCG* ranging from 50 to 925 mgm. One of the calves which had received a single dose of 50 mgm. was tested fifty days after vaccination and died nineteen days later. A second calf was vaccinated twice, the total amount of *BCG* being 60 mgm., and died of tuberculosis twenty-eight days after the test. A third calf which had received 775 mgm. of *BCG* in five doses given during a period of two and a half months died ninety-seven days after the test inoculation of tuberculosis limited to the thoracic organs. The remaining calf, which also received five doses of *BCG*, the

total amount, however, being 925 mgm., exhibited a high resistance. The animal, a heifer, is alive nearly two years after the test and has a calf. Thirty-four calves were vaccinated intravenously, and all except one showed increased resistance, but there were great individual variations in the degree of resistance. One calf which had been given a single small dose of *BCG* exhibited only slightly increased resistance. Thirty-two calves were vaccinated twice, the first dose of 10 mgm. being followed twenty-one to twenty-four days later by 20 mgm. in one instance, 50 mgm. in 7 instances, 75 mgm. in 4 instances, and 100 mgm. in 20 instances. Eleven of the 32 calves died, or were killed when dying, in from thirty-three and a half to seventy-three days of tuberculosis, severe in the lungs and thoracic lymph nodes and slight or not apparent elsewhere. One calf was killed on account of ringworm ninety-two days after the test and showed chronic generalized tuberculosis, not severe. Ten calves were killed because of meningitis a hundred and thirty-two to three hundred and seventeen days after the resistance test; besides tuberculosis of the meninges there were disseminated lesions in other parts of the body, for the most part slight and not progressive. One calf was killed two hundred and forty-five days after the test because of cerebral symptoms, and showed tuberculosis of the bones of the skull and a vertebra, and general nodular tuberculosis, not severe. One calf was killed three hundred and sixteen days after the test because of paralysis of the hind legs; the autopsy showed three tuberculomata in the cord, with secondary involvement in the iliac lymph nodes and no signs of tuberculosis elsewhere. Two calves lived five hundred and seventy and six hundred and thirty-six days after the test; one showed at autopsy examination slight retrogressive tuberculosis, the other moderate general tuberculosis. Five calves are still alive. One calf was vaccinated three times, receiving 5, 10 and 50 mgm., the interval between doses being seven and fourteen days. Tested eight weeks later the calf was less resistant than the controls. These results are much more encouraging than may appear at first sight. It must be remembered that although the test doses employed throughout the experiment were exceedingly severe the life of 23 of the 51 vaccinated animals was prolonged for periods ranging from eight months to three years, and the great majority of the remainder showed definitely increased resistance. There is little doubt that a less severe dose administered, so as to resemble more closely a natural infection, would have given more spectacular results. *Conclusions: 1:* The strain of *BCG* used throughout these experiments would appear to be avirulent for the calf and incapable of giving rise to progressive tuberculosis, even when inoculated intravenously in large doses. *2:* Whether given by mouth or intratracheally, or by subcutaneous or intravenous injection *BCG* can raise the resistance of a calf to a virulent experimental infection. *3:* An increase of resistance is less certain after feeding with *BCG* than after intravenous injection, though feeding with the vaccine may in some instances induce as high a resistance as injection into the tissues. *4:* Intravenous injection has proved the most satisfactory method of vaccination with *BCG*. *5:* The degree of increased resistance conferred upon calves by intravenous vaccination varies within wide limits, and appears in general to be directly proportionate to the dose of *BCG* vaccine.—*The Use of BCG in the Vaccination of Calves Against Tuberculosis, J. B. Buxton and A. S. Griffith, Lancet, February, 21, 1931, ccxx, 393.*—(*F. G. P.*)

Eradication of Cattle Tuberculosis in United States.—Progress in the campaign for eradication of tuberculosis from livestock has been unusually satisfactory during the last 12-month period. It is estimated that in May, 1922, 4 per cent of all cattle in the United States were tuberculous; that in May, 1928, this figure was reduced to 2 per cent and in May, 1930, to 1.7 per cent. The disease exists in 7 per cent of the 3,072 counties in the country, although in nearly one-half of these it is present in less than 1 per cent of the cattle. Reactors were found in 3.3 per cent of 80,000 herds, 78 per cent of the reacting herds being in nonaccredited areas. In New York, state testing of fully accredited herds is done annually. Over 4,000,000 cattle were added to the modified accredited areas during this 12-month period. Michigan has been added to the small list of states in the modified-accredited area. Infection will recur in accredited herds, as shown by the fact that 8,469, or 0.34 per cent, of 2,502,386 retested cattle reacted. At present there are 1,055 counties (34 per cent) in 36 states which are included in the modified-accredited area. Fewer cattle (by 120,000) were tested this year than last, prior to interstate shipment, the incidence of 0.4 per cent of reactors in such cattle being what it was a year ago. There has been a decrease in the value of dairy cattle during the year, as indicated by a substantial reduction in the salvage and appraisal figures which are $20 to $30 per head less. The incidence of tuberculosis found at slaughterhouses is less than a year ago in both cattle and hogs. Out of 8,000,000 cattle carcasses examined, only 0.73 per cent showed tuber-

culosis. Paratuberculosis, or Johne's disease, is fairly widespread but not prevalent. More work is needed to elucidate the nature and better means of detecting this disease. The work in avian tuberculosis eradication has gone along satisfactorily.—*Present Status of Coöperative Tuberculosis Eradication Campaign in the United States, A. E. Wight, J. Am. Veter. Med. Assn., March, 1931, lxxviii (n.s. xxxi), 378.*—(*H. S. W.*)

Sanitation in Eradication of Bovine Tuberculosis.—Great progress has been made in the tuberculin testing of cattle and slaughter of reactors. If this were entirely adequate to suppress the disease, the problem would be much simpler than it is. The test, while highly efficient, is not an absolute indicator, for it does not detect all animals that harbor tubercle bacilli. For instance, severely infected cattle often fail to react; very recently infected animals do not react, and cattle with a healed or calcified lesion may fail to react, but the disease may spread later from the interplay of accessory factors. The first circumstance is circumvented by biannual retesting until a completely negative test is obtained. A system of sanitation is necessary to take care of bacilli which are eliminated through the faeces and contaminate the soil for a long time. Such a system should reckon with the type of soil, the ventilation, type of building, method of handling manure, disinfection, etc. Barns should be clean, light, dry and airy, but not drafty and warm. Nutrition should be maintained. Disinfection of the soil is impracticable. Attention to contaminated barns is of the greatest importance, and detailed instructions for this are available. Numerous problems arise in eradication schemes. One of these is the fact that of reactors that are sacrificed 12 per cent reveal no gross lesions. Gross inspection cannot be expected to find all lesions, but the "no-lesion reactor" is a potent factor in causing discontent on the part of cattle owners. More study is needed into the possibility of other causes than virulent tubercle bacilli for this condition. Another problem is that of whether tuberculosis in cattle can ever be eradicated until more attention is paid to tuberculosis in other farm animals and poultry and in human beings. A third problem is that of the "skin-lesion" infection.—*The Importance of Sanitation in the Prevention and Control of Bovine Tuberculosis, C. L. Hill, J. Am. Veter. Med. Assn., March, 1931, lxxviii (n. s. xxxi), 401.*—(*H. S. W.*)

Control of Bovine Tuberculosis in California.—For 15 years California has enforced a state law which requires that all milk for sale in the state has to be produced by tuberculous-free cattle. The law applies even to the family cow, if her milk is sold or given away. All herds are tested annually; those having had reactors are tested semiannually. During the past year 213,749 dairy cattle (10,229 herds) were tested. Eighty-two per cent of these herds were tuberculosis-free. In several of the counties less than one per cent of the cattle are tuberculous at this time. For nine years, coöperative work in the eradication of tuberculosis has been carried out in areas or counties in which *all* cattle were tested, even over a protest by an occasional owner. An area of 25,000 square miles, containing 250,000 cattle, is now entirely free from the infection. Reactors have been killed and no indemnity has been paid. Now the law authorizes the payment of indemnity. Under the provisions of this law, tuberculin can neither be purchased nor used by any one except licensed veterinarians who are approved by the State Division of Animal Industry. Meat inspectors have aided a great deal in carrying out the scheme of eradication. It is recommended that the American Veterinary Medical Association should advocate the enactment of similar laws for all the states.—*A Review of Tuberculosis Control in California, J. P. Iverson, J. Am. Veter. Med. Assn., December, 1930, lxxvii (n. s. xxx), 725.*—(*H. S. W.*)

Susceptibility of Gopher to Tuberculosis.—In order to determine the anatomical reaction of the thirteen-lined ground squirrel, *Citellus tridecemlineatus* (Mitchell), to the three types of *B. tuberculosis* the following experiment was performed: Twelve adult animals were captured in their natural haunts and divided into three lots, each containing 4 animals. The animals in each lot were inoculated with 0.5 cc. of bacillary suspension, one lot receiving bovine, another avian, and the third human tubercle bacilli recently isolated. With each type of organism two animals were injected intravenously, one subcutaneously, and one intraperitoneally. Two of the 12 animals injected escaped after having been under observation for six weeks and were not recaptured, and one animal died three hours after injection. Of the remaining 9 four died after intervals of from 36 to 78 days and the others were killed for autopsy at from 40 to 91 days after injection. Definite lesions of tuberculosis were observed, the degree or extent of the infection varying with the route of inoculation and most pronounced in the animals inoculated intravenously. Except when injected intravenously avian bacilli produced

fewer lesions than the mammalian strains. The lesions were essentially of the same character as the mammalian, consisting of collections of monocytic cells with a tendency to undergo caseation. The most extensive lesions occurred in those animals which received human tubercle bacilli. The extent and character of the lesions, however, appeared to be quite dependent on the route of inoculation, for although the lesions were exceedingly extensive following the intravenous route, none could be found in the tissues of the gopher (No. 12) inoculated subcutaneously. In the animals which were given injections intravenously well-defined lesions of tuberculosis resulted, regardless of the source of origin of the infecting bacteria. The resistance of the gopher to the avian bacilli, even when given intravenously, was evident from the fact that, even though numerous lesions occurred in the liver of the animal, the lungs were unaffected. This suggests that the lungs of the gopher possess a peculiarly efficient resistance to the avian form of tubercle bacilli, similar to that observed in the lungs of the dog. *Conclusions:* It is impossible to induce lesions of tuberculosis in the striped gopher with each of the three forms of the tubercle bacillus. The animals are more susceptible to organisms of bovine and human type than to avian bacilli. The route of inoculation has a significant bearing on the development of subsequent lesions, the intravenous route being the most effective. The failure to observe lesions of tuberculosis in one gopher, which had been inoculated subcutaneously with human bacilli, would make one hesitate to substitute the striped gopher for the guinea pig for determining the presence of tubercle bacilli by inoculation.—*Susceptibility of the Gopher (Citellus Tridecemlineatus) to Mycobacterium Tuberculosis, W. H. Feldman, Am. J. Path., March, 1931, vii, 139—(J. S. W.)*

Avian Tuberculosis in Mammals.—Examination of material from 105 tuberculous fowls yielded avian tubercle bacilli in 104 instances, the remaining specimen yielding both avian and mammalian bacilli. Birds do not acquire tuberculosis from mammalian tubercle bacilli. Material from 58 cases of generalized tuberculosis in bovines originating in many parts of the United States yielded bovine tubercle bacilli in every instance, while that from 39 cases of "no-lesion" reactors (cattle) yielded no bacilli. Tuberculosis-free pigs failed to develop tuberculin sensitiveness or demonstrable lesions after being fed, months before, with considerable amounts of bovine skin lesions. Material, chiefly solitary lymph nodes, from 115 bovines yielded bovine bacilli in 100 cases, avain bacilli in 11 cases and both bovine and avian bacilli in four cases. Thus an incidence of 12 per cent (plus) of avian infection was found among cattle. Material from 227 cases of human beings with tuberculosis, mostly nonpulmonary, yielded human tubercle bacilli in 217, bovine tubercle bacilli in nine, and avian tubercle bacilli in none. Forty per cent of these 217 people were younger than 15 years, but only two of the 9 instances in which bovine bacilli were found were in this age-group. Ninety-nine of the 227 cases had renal tuberculosis and, of these, six yielded bovine bacilli. It appears that children are "no longer conspicuously exposed to bovine-infection sources." Avian tubercle bacilli do little harm in mammals at present.—*Remarks on Avian Tuberculous Infection in Mammals, L. Van Es, J. Am. Veter. Med. Assn., March, 1931, lxxviii (n. s. xxxi), 371.—(H. S. W.)*

Reaction of Dog to Avian Tuberculosis.—Avian tuberculosis has been observed in many of the common mammals including swine, horses, cattle, and sheep but has never been reported in dogs. Since there are many opportunities for the average farm dog to become infected with avian tuberculosis, its apparent failure to do so must be due to rather definite factors. It has been shown by the author, however, that when these organisms are injected directly into the cerebral substance there results a definite tuberculous infection which is usually fatal. Also, when large numbers of the organisms are introduced directly into the blood-stream, mild tuberculous lesions occasionally occur. In the present article a detailed account of the pathological changes observed in these former experiments is given. The infecting agents used were emulsions prepared from the liver and spleen of chickens dead from tuberculosis, or suspensions of avian tubercle bacilli. Six adult dogs received intracerebrally 1 cc. of a heavy suspension of avian bacilli. Three different strains of this organism were used and 2 dogs were injected with each strain. All dogs given intracerebral injections died 17 to 29 days after inoculation and definite tuberculous lesions were found in the brain and liver in every instance. In only one animal was the spleen involved, and the lungs escaped demonstrable infection in each case. Also, 10 adult dogs were injected with avian bacilli by way of the jugular vein. Only one died spontaneously; the others were killed for autopsy over a period of a hundred days to one year after injection. In only one of the animals were lesions demonstrated which could be con-

sidered of a definitely tuberculous nature. In three others, however, a few lesions were observed, which were histologically identical with those of tuberculosis, although acid-fast organisms were not found among the cells constituting the respective lesions. The lesions in three of these 4 animals were entirely confined to the liver and were microscopic. With one possible exception, in none of the 10 animals were lesions found grossly or microscopically in the lungs, spleen or kidneys. The information at hand seems inadequate to explain satisfactorily the consistent and extensive infection of the liver in the intracerebrally inoculated animals, in contradistinction to the infrequency of lesions in the liver of the dogs inoculated intravenously. Likewise the failure of the disease to become manifest in the lungs, irrespective of the route of infection, is difficult to explain and emphasizes the significance of the susceptibility of organs in the pathogenesis of tuberculosis. The lesions induced in the pia mater were essentially circumscribed or diffuse accumulations of monocytic cells, with no tendency to tubercle-formation. The lesions in the livers of dogs infected by the cerebral route consisted of multiple, discrete collections of monocytic cells in the substance of the various lobules of the liver. The majority of these lesions were vigorously proliferating, although necrosis was not common. The apparent absence of giant cells in all lesions would indicate that these structures are not a part of the histological response of the dog toward tuberculous infection. Although the dog's brain offers a vulnerable portal of entry for the subsequent development of a tuberculous process from avian bacilli, an attempt to establish an infection with this organism by another route brings out the fact that the dog possesses an extremely formidable constitutional resistance to this form of the disease.—*The Pathological Changes Following Experimental Exposure of Dogs to Mycobacterium Tuberculosis of Avian Origin, W. H. Feldman, Am. J. Path., March, 1931, vii, 147—(J. S. W.)*

Pseudotuberculosis in Laboratory Animals.—In 1929 a disease simulating tuberculosis superficially appeared in the stockroom of small laboratory animals of the Animal Diseases Research Institute in Ottawa. It affected a few rabbits only, but it became enzoötic among guinea pigs. It led to the death of many animals in widely separated cages without giving evidence of direct transmission from one to another. It produced characteristic pathological changes, particularly in the spleen and often in the liver. These organs were "studded with foci varying in size from minute white points, barely discernible, to yellowish-white or whitish-yellow nodules projecting above the surface and measuring several millimeters in diameter." Changes were present throughout the depths of the tissue. The spleen was usually considerably swollen. The reacting tissue in its earlier stages resembled early miliary tuberculosis, but in the later stages this resemblance to tuberculosis was not nearly so striking. In section the nodules appeared as having a thin fibrous capsule and a content of thin, homogeneous, semitranslucent material in definite contrast to the dry caseous material of the tubercle. In the acute cases animals died before focal necrosis developed, with marked swelling of the spleen as the only grossly demonstrable sign of disease. Several stillborn guinea pigs showed this. There was but little if any lymphatic involvement. A specific microörganism was readily recoverable from the typical lesions, the blood, bone-marrow and diseased viscera, and was never found in healthy animals. This bacterium is a relatively small gram-negative bacillus. It grows well on ordinary media, except potato, as grayish white, smooth, moist, opalescent colonies. It does not liquefy gelatine. It causes turbidity in broth. It forms acid and gas in dextrose, galactose and manuose, but not in lactose. It has no characteristic odor. It is a small bacillus with rounded ends and may grow singly, in pairs or sometimes in short chains; it is aerobic and motile and grows at 37°C., but not at room temperature. Normal guinea pigs would not be infected by being fed this bacillus for several days but succumbed from subcutaneous and intraperitoneal inoculation. Chickens are susceptible. Sera of infected guinea pigs and rabbits have a high agglutinative titer. Sera of infected rabbits agglutinate type strain *Salmonella enteritidis*. The animals do not react to tuberculin. Of 856 autopsies in this laboratory during the year, no instance of spontaneous tuberculosis was observed.—*Salmonella Enteritidis Infection in Guinea Pigs and Rabbits, R. C. Duthie and C. A. Mitchell, J. Am. Veterin. Med. Assn., January, 1931, lxxviii, (n. s. xxxi), 27.—(H. S. W.)*

Review of Ranke's Classification.—It is well understood that immunity and allergy in tuberculosis rest on infection. The first infection leads to caseation or miliary spread, whereas in the subinfection there is a limited spread, for the dissemination of the tubercle bacillus seems to be made difficult. The most important applications of the allergy-conception is expressed in Ranke's

theory which recognizes the fundamental difference in primary and postprimary course. The postprimary course may consist of (1) heightened susceptibility in generalization and metastases or (2) also decreased susceptibility in the form of isolation of the process to one organ. Ranke has classed the disease into three stages: the primary complex, the secondary stage and the tertiary stage. The primary complex may be found in 70 to 80 per cent of the cases. The simultaneous and obligatory lymph-node involvement at the root of the lung in the human being is very characteristic. If the primary focus is in the intestines, the bronchial lymph nodes are free in spite of extensive haematogenous pulmonary change. The primary complex occurs only once and is mostly singular. The primary complex produces and sustains a condition of changed reaction to the virus (allergy). Negative tuberculin tests are to be evaluated only if used separately in a 1/10 dilution. The secondary stage of Ranke comprises changes which are propagated from the primary focus haematogenously, special forms of this generalization being represented by tuberculous pneumonia and meningitis and miliary tuberculosis. The third stage comprises 70 to 80 per cent of all cases of tuberculosis and is characterized by the absence of peripheral metastases, which expresses a relative immunity, the predominance of intracanalicular metastases such as is shown by laryngeal and intestinal tuberculosis. The isolated phthisical lesion may originate often on the basis of haematogenous foci (endogenous reinfection).—*Immunitaetsvorgaenge. Ihre anatomischen Grundlagen und ihre Bedeutung für den Ablauf der menschlichen Tuberkulose., W. Pagel, Deutsche med. Wchnschr., December 12, 1930, lvi, 2119.*—(*H. S. W.*)

Tissue Reactions in Tuberculosis.—The entire concept of the pathology of tuberculosis has been revised since the introduction of the newer methods of studying appropriately stained living tissues. Criteria have been established for the recognition of the individual epithelioid cell when entirely separated from all other structures or cells. This has led to the following studies: *1:* The study of the white blood cells in tuberculosis. The peripheral blood was examined in rabbits in which the tuberculous process was advancing rapidly, and a very marked increase in the circulating monocytes and a marked decrease in the circulating lymphocytes were found. These changes were, however, reversed in those animals which recovered from the infections. The hypothesis was suggested that the monocyte-lymphocyte index, or the ratio existing between these cells, indicated quite definitely the general condition of the animal. The ratio in the average normal person is 0.3. Ratios from 0.6 to 1.0 usually indicate active tuberculosis, and a ratio of more than 1.0 indicates marked severity of the condition. Medlar's conclusions are: "The neutrophile plays the chief rôle in tuberculous abscess-formation and in the extension of tuberculous ulcers. Rupture of abscesses and erosion of the walls of cavities are liable to give rise to hemorrhages or to marked 'spreads' of the disease to new tissues. The mononuclear leucocyte is the chief cell in new tubercle-formation, and the lymphocyte predominates when a tuberculous lesion is healing. No definite rôle can be ascribed, at present, to the eosinophile or basophile." *2:* The study of the tissue cells from tuberculous animals has given rise to more careful identification and a better concept of the interrelationship of different members of the connective tissue cell group found in tuberculous lesions. Experimental work has shown that the presence of tubercle bacilli called forth a great overproduction of the reticular or primitive type of cell and a rapid conversion of these cells into monocytes, and finally into epithelioid cells. Observations indicate that the epithelioid cells are unable to digest bacilli. The monocytes digest bacilli, but their cytoplasm becomes a favorable medium for their further development. The epithelioid cell is characterised by a larger number of minute droplets which stain with neutral red, by an accumulation of fatty droplets in the cytoplasm, and by the presence of tubercle bacilli which are obviously alive. The cells from which the epithelioid cells are derived always contain larger and more irregular vacuoles, and as a rule give other evidence of a more marked capacity to phagocytose foreign material. It may be assumed that monocytes and clasmatocytes, in tuberculous infections, ingest tubercle bacilli and as a result of the presence of these organisms pass into the epithelioid type of cell. This may be interpreted as a definite change in the general physiological reaction of these cells. It is believed that the giant cells found in tuberculous tissues are formed from typical monocytes and epithelioid cells by a process of division of nuclei without division of cytoplasm, although there are indications that fusion of cells may take place, furnishing giant cells by this means. The recent studies point out that the entire trend of events has been dependent upon two observations: (a) the specific differentiation of the epithelioid cell by new criteria; and (b) the observation that these cells are

not normal characteristic entities, but rather physiological degeneration forms resulting from more than one type of normal cell. Certainly, the concept that tuberculosis is primarily characterized by the presence of degenerating cells which are, in all probability, capable of harboring bacilli directly as a result of these changes, leads us to postulate the future studies of tuberculosis as being necessarily dependent upon the search for methods to controvert this peculiar degeneration. *3:* The blood and tissue cells have been used as biological tests for the study of chemical fractions obtained from tubercle bacilli. It has been found that the protein fractions produce toxic symptoms in rabbits. The various lipoid constituents apparently represent the active fractions of the organism in so far as its production of the specific changes in cells and tissues characteristic of tuberculosis is concerned. *4:* The morphological characteristics determined supravitally in tuberculous tissues have been studied with regard to their possible physiological character, and efforts have been made to analyze the meaning of these changes. Experiments have been instituted to confirm these conclusions and to analyze the possibility of controlling them. These experiments have led to the study of the nonspecific production of epithelioid cells, the modification of epitheloid cells and their replacement by more active types. Certain nonspecific substances, such as phosphorus, agar, mercury, oils and salt solutions, produce also the characteristic cells found in tuberculous processes. *5:* The experiments on tuberculosis suggested the analysis of other diseases in which the tissue reactions had been found to be morphologically similar, resulting so far in a better knowledge of syphilis and promising equally interesting results in other conditions. The tendency of these investigations suggests that the primary characteristic of the tuberculous pathological process is a decreased metabolic activity on the part of the tissue cells involved. This is specifically contrasted with the findings in syphilis, in which the opposite is true.—*Recent Developments in the Study of the Tissue Reactions in Tuberculosis: a Review, R. S. Cunningham, Tubercle, June, 1931, xii, 404.*—(*M. E. P.*)

Experimental Tuberculosis.—In animals which are otherwise resistant to tuberculosis or to certain strains of tubercle bacilli, lesions may be produced by intracerebral inoculation. Utilizing this additional method of inoculation when necessary, lesions were produced by tested strains of avian, bovine and human tubercle bacilli in chickens, guinea pigs, rabbits and dogs. Tuberculous infection in the tissues of the chicken, when induced by any of the three forms of the tubercle bacillus, was characterized by the appearance of definitely focal, circumscribed collections of monocytic or epithelioid cells of a rather large clear type. The lesions which are often multiple, may become confluent, but, even though a conglomerate tubercle results, the identity of the separate follicle-like masses of epithelioid cells is usually maintained and is discernible. In the guinea pig the lesions were all similar and were characterized in their earlier stages by closely arranged, diffuse masses of monocytic cells, disposed in an irregular manner, and in this regard they differed materially from the lesions produced by the same organisms in the chicken. The lesions in the rabbit were all characterized by the formation of irregular masses of monocytic or epithelioid cells, and the central portion of many became caseated within a relatively short time. Giant cells were numerous, and encapsulation was not apparent. In the dog slight differences were observed in the lesions produced by each of the three types, but these were perhaps due to the anatomical peculiarities of the involved organs. The lesions were characterized by the presence of monocytic cells arranged in compact masses without evident encapsulation or typical tubercle-formation. The lesions, which were rather extensive and numerous, showed only a slight tendency toward retrogression. It would seem that the differences of histological detail assumed by the resultant reactions of tissue to the respective types of tubercle bacilli are determined for the most part by factors inherent in the host rather than by the possession by each of the three bacillary forms of certain lesion-inciting constituents which are specific for it. The type of bacillus in a lesion can only be determined by the appropriate pathogenicity tests on animals.—*The Histology of Experimental Tuberculosis in Different Species, W. H. Feldman, Arch. Path., June, 1931, xi, 896.*—(*R. D.*)

Early Infiltration.—The early infiltration is defined as the appearance of rather large homogeneous shadows in the lung at the onset or during the course of pulmonary tuberculosis. They are caused either by a bronchogenic aspiration, following an exogenous or endogenous infection or by an allergic infiltration around older foci. They are frequently found in the infraclavicular region, they are round or wedge-shaped, and in the latter case they are frequently delimited in the lower part by the intralobar fissure. They may remain unchanged for some time or they may show central excava-

tion, which may occur very rapidly. Only a part of these lesions cause definite symptomatology while a large part remain subjectively unnoticed. Some start with high temperature and all the symptoms and signs of influenza. Sputum examination may demonstrate tubercle bacilli shortly after the onset of symptoms; the physical signs are usually not characteristic until one or two weeks after the onset. Other patients show the same roentgenological findings with only slight symptomatology of low-grade fever and slight general malaise. The early diagnosis of these lesions is very important because many of them need immediate pneumothorax treatment in order to prevent further spread. In children who are exposed to tuberculosis one finds not infrequently broad parahilar or paratracheal infiltrations which are probably due to a collateral inflammation around tuberculous lymph nodes. The early infiltration is particularly important as an acute phase in the course of tuberculosis, both at the onset or during the latter acute exacerbation. Since many infiltrations occur without or with atypical symptoms they are frequently overlooked.—*Welche Bedeutung hat das moderne Frühinfiltrat für die Diagnose und Prognose der Tuberkulose? W. Neumann, Wien. klin. Wchnschr., October 23, 1931, xliv, 1348.*—(*M. P.*)

Nature of Alveolar Phagocytes.—Extensive histological studies on the lungs of bats which showed marked deposits of pigments, both within fixed and free cells, led to the conclusion that the alveolar phagocytes are of histiocytic and not of epithelial origin.—*Bemerkung zur Frage nach der Natur der Alveolarphagozyten in der Säugetierlunge, J. Mathis, Wien. klin. Wchnschr., July 3, 1931, xliv, 885.*—(*M. P.*)

Death in Chronic Pulmonary Tuberculosis.—This is a detailed discussion of the causes which finally lead to death in chronic pulmonary tuberculosis. The differentiation is of some practical significance because it affords a guide for that symptomatic treatment which may render the patient more comfortable in the terminal period. Death may be due to a cessation of function of the heart, the lungs or the brain, or it may be death from inanition.—*Der Tod an chronischer Lungentuberkulose, A. Sattler, Wien. klin. Wchnschr., August 7, 1931, xliv, 1016.*—(*M. P.*)

Vital Capacity.—A comparative study of students, whose vital capacity was more than 15 per cent above or below the average of their heights, was made to determine whether the group with low vital capacity showed signs of disease, and whether, also, there were indications that vital capacity is an important function for judging physical fitness. These students were found in 5 freshman classes at Mount Holyoke College. There were 121 with high vital capacity and 85 with low vital capacity. Two classes were studied for four years, with two conferences each year for each student. The other classes were studied for shorter periods, as their year of entrance made possible. While in a few instances there seemed to be direct association of low vital capacity with past or present disease of the thorax, heart or lungs, the majority of these students seemed to be young women for whom the exercise program in the years previous to college was very limited. The response of 22 students in one class, which has been specially trained for thoracic development, was gratifying. By whatever test this low-vital-capacity group was tried out, by the test of general health, of academic or of social success, it appears that it was truly at a disadvantage. There is thus the indication that vital capacity is a measurable function of significance in the general picture of the young women whose relative success in the field of health one is anxious to rate fairly. Two "morals" appear: one, the importance of sturdy exercise for girls, especially in their adolescent years; the other, the opportunity of bettering the low vital capacity and with it the general health of at least many of this group of students during their college year.—*Vital Capacity in College Women, A. H. Turner, Arch. Int. Med., December, 1930, xlvi, 938.*—(*W. I. W.*)

Exudative Diathesis in Respiratory Infection.—The exudative lymphatic diathesis of Czerny is thought to be due mainly to improper feeding, particularly from overfeeding of fat, but it has been found following measles, whooping-cough and scarlet fever in children who had had a properly regulated diet. It is characterized by a certain periodicity and vicious cycle, because a catarrhal condition from one part causes a catarrh in some other part of the respiratory tract. Part of these exudative reactors with chronic catarrh have a similar symptomatic complex (fever, exhaustion, loss of appetite, vasomotor disturbances), such as may be caused by tuberculosis. These symptoms should be conceived of as a general reaction of the body in the sense of an especially increased tuberculin sensitization, to which this type of child is susceptible. In spite of the inflammatory "readiness," these individuals show a marked relative immunity to tuberculosis.—*Ueber die sogen-*

annten banalen Infektionen der oberen Luftwege im Kindesalter, Schlack, Deutsche med. Wchnschr., November 7, 1930, lvi, 1907.—(H. S. W.)

Movements of Lung.—A method for measuring certain movements of the lung is described. This method was employed in the examination of 2 patients with healthy lungs, and of two with pulmonary tuberculosis in whom phrenic evulsion was performed. In the normal lung, it was found that on inspiration all parts of the lung are lowered vertically, the base descending much more than the apex. The degree of expansion of the lower area seems usually higher proportionately than the degree of expansion of the upper area of the lung. On inspiration the apex moves outward. In other parts, although expansion of the infundibula causes an outward enlargement, there appears to be a drawing in of the bronchial tree toward the midline, the vertical branches of the bronchi tending at the same time to move toward the horizontal. After evulsion of the phrenic nerve, the apex appears unaffected. The downward movement of the midpart of the lung is considerably lessened. The vertical movement at the base is either practically abolished or else there is a movement in the reverse direction, slightly upward on inspiration (paradoxical). The drawing in of the bronchial tree toward the midline is seen as in the normal lung, but the movements have been modified. The tendency seems to be toward an increase of the movement towards the midline due to mediastinal excursion from the diaphragm action on the sound side. This may be due to pleural adhesions. Evulsion of the phrenic nerve affects the respiratory movements of the base of the lung very greatly, the movement of the middle part appreciably, and those of the apex negligibly. Evulsion is not likely to benefit tuberculous disease that is truly confined to the upper lobe, except by means of alleviating cough or other subsidiary symptoms.—*Certain Movements of the Lung and the Effects of Phrenic Evulsion thereon, C. A. Sprawson, Tubercle, May, 1931, xii, 337.—(M. E. P.)*

Filterability of Tubercle Bacillus.—Fresh sputum, containing large numbers of tubercle bacilli was collected and incubated for 48 hours at 37°C. After 0.1 and 0.01 cc. of this was inoculated respectively into two guinea pigs, the sputum (to which was added a culture of *B. prodigiosus* to test the permeability of the filters) was passed through a Berkefeld filter (and similar specimens were similarly treated and passed through a Seitz filter). The filtrate in each instance was cultured for *B. prodigiosus*, and then stored in the ice-chest over night before it was inoculated into healthy, nonreacting (tuberculin) guinea pigs. Altogether, 43 guinea pigs were inoculated: 10 with a Seitz filtrate, 22 with a Berkefeld filtrate, and 11 with a filtrate which had passed through both a Seitz and a Berkefeld filter. In no instance did the animals develop any signs of tuberculosis; none revealed tubercle bacilli when their tissues, especially the tracheobronchial lymph nodes, were examined in smear; none showed any emaciation. The control animals that had received small amounts of the unfiltered specimens of sputum died with generalized tuberculosis.—*A Study of the Effects on Guinea Pigs of Seitz and Berkefeld Filtrates of Sputum from Tuberculous Patients, A. Larson, J. Prev. Med., March, 1931, v, 161.—(H. S. W.)*

Serological Differentiation of Human and Bovine Tubercle Bacilli.—In spite of many previous failures attempts were renewed to differentiate the human and bovine types of tubercle bacillus by immunological methods. A differentiation is impossible by tuberculin reactions, using either tuberculin or bacillary suspensions of human and bovine strains. No known antigenic fraction of the tubercle bacillus produces a type specific serum. Human sera cannot be differentiated with type-specific antigens in complement fixation. Certain sera from tuberculous cattle react only with bovine antigens in complement fixation, using lipoidal extractions. A definite differentiation between human and bovine types of tubercle bacilli has not been possible.—*Versuche zu einer immunbiologischen Differenzierung des Typus Humanus und Typus Bovinus des Tuberkelbacillus, F. Klopstock, Klin. Wchnschr., May 23, 1931, x, 966.—(M. P.)*

Modification of Cream Medium for Tubercle Bacilli.—The cream medium advocated by Sweany and Evanoff is good but is technically difficult to prepare. A modification has obviated this difficulty and has not detracted from the high quality of the medium, which, then, is prepared as follows: 250 gm. of freshly ground lean steak is added to 100 cc. of distilled water and soaked in the icebox over night when it is autoclaved. To 100 cc. of this, 50 cc. each of sterile cream and sterile whole milk and 400 cc. of whole eggs are added, and the mixture is well stirred and strained through gauze. It is then tubed and sterilized fractionally at 75°C. for one hour for 4 days and then incubated for 2 or 3 days. Prepared

in this way the medium is excellent both for isolation and for carrying routine cultures of tubercle bacilli.—*A Modification of the Medium of Sweany and Evanoff for Culturing the Organism of Bovine Tuberculosis, W. H. Feldman, J. Am. Veter. Med. Assn., April, 1931, lxxviii (n. s. xxxi), 527.—(H. S. W.)*

Malaria and Resistance to Tuberculosis.—It is a well known fact that tuberculosis does not spread rapidly in the malarial countries of the tropics. In Java, allergic natives, after being tested with Old Tuberculin, become transiently nonallergic during the development of symptoms of malaria. In patients with malaria, the Wassermann reaction of the blood may be inconstant but that of the spinal fluid is not so. On the other hand, when Old Tuberculin is used as an antigen for the complement-fixation test during an attack of malaria, the reaction is positive in the spinal fluid.—*Zur Frage des Einflusses der Malaria auf den Widerstand des Organismus bei Tuberkulose, H. Heinemann, Deutsche med. Wchnschr., December 26, 1930, lvi, 2213.—(H. S. W.)*

Reactions in Tuberculous Guinea Pigs Sensitized with Various Antigens.—Tuberculous guinea pigs, sensitized with egg-white and also with various other antigens, often die after intraperitoneal injection in a protracted shock which is similar in many respects to tuberculin shock. A strong haemorrhagic reaction develops around the tuberculous lesion. This reaction is not the result of the special sensitiveness of the lesion, for it may be present in any inflammatory area without regard to the origin of the inflammation. The egg-white shock differs in two points from tuberculin shock. The symptoms often begin to develop early after the injection, and in the early phases of the reaction and in the slight reactions a drop of temperature is usually present. These differences are probably connected with the presence of the usual anaphylactic sensitiveness after treatment with egg-white. When the latter is associated with tuberculin sensitiveness, tuberculin shock often presents the same temperature curves and early onset of symptoms as does egg-white shock. The capacity to react with severe protracted shock develops later after the treatment than does either the tuberculin type of skin sensitiveness or anaphylaxis. It was observed in actively sensitized guinea pigs, and the experiments to transfer it passively remained unsuccessful. The different manifestations of the hypersensitive condition develop in a large measure independently from each other. The independence of the severe protracted shock from anaphylactic shock is shown also by the observation that desensitization to acute anaphylactic shock does not interfere with the development of the severe protracted shock. The severe protracted egg-white shock and tuberculin shock are probably analogous processes, but without a more thorough understanding of the physiological mechanism of the reaction this conclusion must be regarded as only provisory.—*Comparative Study of the Anaphylactic and Tuberculin Types of Hypersensitiveness. I. General Reactions Similar to the Tuberculin Shock in Tuberculous Guinea Pigs Sensitized with Various Antigens, L. Dienes, J. Immunol., March, 1931, xx, 201.—(J. S. W.)*

Anaphylactogenic Action of Protein from Acid-Fast Bacteria.—Ordinarily, bacterial preparations are found to be poor antigens, especially as anaphylactogens, and the opinion prevailed at one time that they were entirely inactive in this respect. This is undoubtedly explained by the fact that in their native state bacterial proteins are very insoluble and, when brought into solution, they are either denatured, altered, or hydrolyzed by the manipulations used to dissolve them. But, when the conditions are such that the proteins are procurable by methods that are not drastic, they are found to have antigenic abilities comparable to other proteins known as active antigens. The method devised by the authors for isolating the proteins of tuberculin consists of growing the tubercle bacilli in a synthetic fluid medium for six to eight weeks, removing the bacteria by filtration through Berkefeld filters, and obtaining the proteins either by ultrafiltration and washing or by precipitation with ammonium sulphate, either of which processes yields a concentrated final product that is apparently in the same chemical state as it was in the original culture, since it exhibits the entire antigenic properties, as far as the tuberculin reaction goes, of the entire tubercle-bacillus filtrate. The ultrafiltered product is a solution whose protein content can be assayed. The ammonium-sulphate precipitate is a light brown powder, readily soluble in sodium-chloride solution, forming a perfectly clear liquid. It is to be noted that both products give strong Molisch reactions, indicating the presence of carbohydrate. At the time of the experiments it was not possible to obtain undenatured protein free from carbohydrate in sufficient amount for the tests. The protein preparations were obtained from cultures of human, avian and bovine tubercle bacilli, and timothy bacillus on Long's synthetic medium. The anaphylactic experi-

ments were performed solely with the purpose of studying the antigenic relations of a group of typical whole proteins derived from biologically related sources in much the same manner as isolated proteins from other related sources have been studied. In the experiments no injections of more than 20 mgm. of protein were given, as doses (intravenous) higher than this were often toxic for normal animals. Although anaphylactic death usually occurred within a few minutes and seldom after one hour, the animals were observed for twenty-four hours and all symptoms or deaths occurring after that time were attributed to the primary toxicity of the proteins and not to anaphylaxis. A series of guinea pigs was sensitized by the intraperitoneal injection of the four different proteins in amounts ranging from 0.1 to 15 mgm. After the proper incubation period they were given intravenous injections of the homologous protein in amounts of from 5 to 15 mgm. The results show that these proteins are very active in producing anaphylactic sensitization and shock. The anaphylactogenic action of tuberculin protein was further shown by experiments employing the more sensitive methods of Schultz-Dale and Koessler and Lewis, which show, respectively, the reaction of the sensitized uterine and bronchial smooth muscles. Having therefore established the fact that the isolated tuberculin protein is anaphylactogenic, we are able to compare the reactions of animals directly sensitized with this substance with those of animals infected with tuberculosis. These experiments would show, first, whether the conditions associated with infection lead to true anaphylactic sensitization and, secondly, whether the antigenic substance produced by the tubercle bacillis *in vivo* is the same as that produced *in vitro*. For this purpose a series of guinea pigs was infected with 2 to 2.5 mgm. of live human tubercle bacilli. After periods of infection ranging from two to eight weeks these animals were injected intravenously with 10-mgm. doses of the various tuberculin proteins. The results showed that tuberculous infection may be associated with acute lethal anaphylactic sensitization to tuberculin protein, for 8 out of 10 animals succumbed to the shocking dose in sixteen hours or less, some only surviving a few minutes. That these results were due to true anaphylaxis and not to a tuberculin reaction was amply shown by the Schultz-Dale technique and the Koessler-Lewis bronchospasm method. The mutual sensitizing properties of the four protein preparations were studied with both the gross anaphylaxis method and the uterine-strip technique, the latter being more adapted for studying desensitization. With the gross anaphylactic test, sensitization with one tubercle-bacillus protein produced fatal sensitization to the other two, but did not sensitize to the protein of the timothy bacillus, nor did timothy-bacillus protein sensitize to the tuberculin proteins. The same facts were disclosed with the sensitized uterine-strip preparations, and the further fact was shown that a uterus sensitized to one tuberculin protein reacts when exposed to another, but that some sensitization remains to the homologous protein after desensitization to the heterologous protein. Thus, it is indicated that tubercle-bacillus proteins are closely related, inasmuch as they mutually sensitize to each other. On the other hand, they are dissimilar to the extent that none of them can desensitize a tissue to the protein used for sensitization except the homologous protein. No antigenic relationship whatever was found between the acid-fast tubercle bacilli and the equally acid-fast timothy bacillus. One can conceive that each of these tubercle-bacillus proteins contains one group specific for the organism and another group which is common to the three types of tubercle bacilli. Although usually a poor producer of precipitins, when immunized with tubercle-bacillus protein guinea pigs respond with prodigiously high titres of precipitins. Since it is precipitating serum that is usually used for passive sensitization, on which is based the theory that precipitins and anaphylactic antibodies are identical, it was believed that these precipitating guinea-pig sera would be found to be equally adapted to passive sensitization. Actively precipitating sera were therefore obtained from guinea pigs immunized by repeated injections of human tuberculin protein and injected intravenously into normal animals in various amounts. After an incubation period of twenty-four hours, these guinea pigs were injected intravenously with antigen. Passive sensitization was found to be effectively produced by these antisera. Under certain conditions, the serum of guinea pigs infected with tuberculosis contains high titres of precipitins for the tuberculin protein. In contrast to precipitating sera from guinea pigs immunized artificially with tuberculin protein these sera had little or no passive sensitizing action. By using the uterus-strip technique an indication of a feeble sensitiveness was obtained. On the basis of the possibility that tuberculous serum might contain an inhibiting body or some antigenic substance that acts by blocking the fixation of sensitizing antibody, a single experiment was made to find if tuberculous serum prevented passive sensitization with a known actively sensitizing antituberculin protein

serum. This experiment failed to show any inhibitory effect of the tuberculous serum. *Conclusions: 1:* The proteins isolated from filtrates of acid-fast bacterial cultures on a synthetic medium are actively anaphylactogenic. *2:* By use of the anaphylactic reactions it can be shown that a definite antigenic relationship exists between the three types of tubercle bacilli proteins and none between the tubercle bacilli and the timothy bacillus. *3:* Guinea pigs infected with human tubercle bacilli are actively sensitized to tuberculin protein. This sensitization appears four to six weeks after infection. *4:* Precipitating sera from guinea pigs immunized with tuberculin protein can passively sensitize normal guinea pigs. Precipitating sera from tuberculous guinea pigs are very feeble in their passive sensitizing ability despite their marked precipitin titres.—*The Chemical Composition of the Active Principle of Tuberculin. XII. The Anaphylactogenic Action of the Protein from Filtrates of Acid-Fast Bacteria, J. H. Lewis and F. B. Seibert, J. Immunol., March, 1931, xx,* 201.—*(J. S. W.)*

Skin Reactions with Human Tubercle-Bacillus Protein.—In 1929 Masucci and McAlpine succeeded in isolating a protein from the filtrate of cultures of the human tubercle bacillus H37, grown on Long's synthetic culture medium, and free from the polysaccharide which is usually closely associated with the protein. This protein has been designated '*MA-100*. These investigators also obtained the specific polysaccharide free from the protein. The present communication deals with the skin sensitivity of man to protein MA-100, when the protein is introduced intracutaneously. Tubercle protein MA-100 when injected in this way (in proper dosage) elicits in the majority of adults a skin reaction, reaching its height usually in 24 to 48 hours and indistinguishable from that produced by Old Tuberculin, but apt to be less intense both in coloration and oedema, and more transitory. The reaction is usually an erythema surrounding an area of oedema. As a rule the skin over the oedematous area shows a darker red coloration, but in intense reactions this may be blanched. Subsequent pigmentation, although it occurs, is less apt to follow the protein. One curious feature is that the character of the reaction on the same patient, as to variations of erythema and oedema, is apt to be the same with both materials. Delayed reactions may occur. A safe dosage was found to be 0.000,01 cc. for the Old Tuberculin and 0.000,5 mgm. for the protein. In the majority of individuals tested these doses gave comparable reactions of between 10 and 20 mm. in diameter. The dose of the protein was calculated from the nitrogen content of the material. The solutions were so diluted that 0.05 cc. contained the amount called for and this amount was injected intracutaneously in the usual manner. Readings were made at the end of one and two days and, if no reactions were apparent, a second injection was made, using 0.1 cc. of the same dilutions, thus doubling the dose. The Old Tuberculin used in the study was obtained from Dr. M. Dorset, Chief of the Biochemic Division of the United States Bureau of Animal Industry. *Incidence of the Skin Reaction:* In 204 cases of pulmonary tuberculosis, having tubercle bacilli in the sputum, the incidence of the reaction with protein was 94.1 per cent and 90.6 with the Old Tuberculin, a difference of 3.5 per cent in favor of the protein. In 57 cases, with a clinical diagnosis of tuberculosis, but with negative sputa, the percentage of reactions was 92.9 with the protein and 91.2 with the Old Tuberculin. In 137 adult ward-patients in two Philadelphia hospitals, all clinically nontuberculous, 81 per cent gave reactions with the protein and 71.5 per cent with the tuberculin. Twenty-five sanatorium cases, clinically nontuberculous (pneumonoconiosis, bronchiectasis, etc.) gave 68 per cent positive with the tuberculin and 80 per cent with the protein. A group of children, 43 in number, varying in age from one to twelve years, and with an average of 5.3 years, gave 16.2 per cent positives with the tuberculin and 25.5 with the protein. It is striking that in this group the percentage of difference in the incidence of reactions to the two test materials is about identical with that of the clinically nontuberculous adult group. Based on these observations it is concluded, tentatively, that, in active tuberculosis the percentage of reactions obtained with the two test materials tends to approach a mean, with a slight difference in favor of the protein. In latent tuberculosis, however, there is a marked difference in favor of the protein, more cases being picked up with the protein than with the tuberculin. A small group of noncorrelated reactions is reported, in which there are 10 cases reacting definitely with the MA-100 protein *only*, of which 6 had tubercle bacilli in their sputum and 2 cases, both with positive sputa, giving reactions with the tuberculin and not with the proteins. These results were surprising in view of the fact that Old Tuberculin is a complex mixture, presumably carrying most or all of the react-

ing substances derived from the tubercle bacillus and that the human tubercle bacillus protein MA-100 is, in comparison, a simple substance. A certain small number of known tuberculous individuals fail to react to either the tuberculin or the protein. Some are perhaps too ill to react, but why others, in fairly good condition, fail to react is not understood. The possibility that repeated injections of the MA-100 protein may produce in time a skin sensitivity to the material that is not related to the presence of tuberculous infection is discussed. The possibility of such sensitization is admitted but there is no very definite evidence that it occurs. *Conclusions:* As a diagnostic agent human tubercle bacillus protein MA-100 is as good as and possibly better than Old Tuberculin, especially in view of the fact that the protein is a pure substance as compared to the very complex composition of the tuberculin.—*Brochemical Studies of Bacterial Derivatives. XI. Skin Reactions in Man with Human Tubercle Bacillus Protein MA-100. Preliminary Report, E. H. Funk and F. M. Huntoon, J. Immunol., August, 1930 xix, 237.*—(*J. S. W.*)

Thyroxin and Tuberculin Allergy.—It was found that several patients who undoubtedly had active pulmonary tuberculosis reacted very slightly or not at all to tuberculin. An analysis of these hypoallergic cases showed that they all had a marked anaemia, a high sedimentation rate, decreased alkali reserve and decreased basal metabolic rate. All these changes were interpreted as being due to hypofunction of the thyroid gland. Thyroid medication proved the point. The above noted haematological and metabolic alterations returned to normal and the tuberculin tests made after the treatment showed strong reactions according to the pulmonary condition. It was noted that the thyroid medication had never any ill effect but that it influenced favorably so called toxic phenomena, such as headache, menstrual disorders, hyperacidity and hypermotility of the stomach and spasms in the gastrointestinal tract. It is concluded that a normal function of the thyroid gland plays a significant rôle in allergy.—*Thyroxin und Tuberkulinallergie, P. Kallos, Klin. Wchnschr., July 25, 1931, x, 1404.*—(*M. P.*)

Key to Abstractors

R.D.: Richmond Douglass, Loomis, New York.
G.L.L.: George L. Leslie, Howell, Mich.
U.E.Z.: U. E. Zambarano, Providence, R. I.
M.E.P.: M. E. Parker, Kalamazoo, Mich.
M.P.: Max Pinner, Tucson, Arizona.
H.J.C.: H. J. Corper, Denver, Colo.
H.S.W.: H. S. Willis, Northville, Mich.
W.I.W.: Walter I. Werner, Pontiac, Mich.
M.D.: Max Deutch, St. Louis, Missouri.
J.P.B.: Joseph P. Bobbio, Northville, Mich.
F.G.P.: Frank G. Petrik, Loomis, New York.
J.S.W.: J. Stanley Woolley, Loomis, New York.